4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA-2011-P-0743 and FDA-2011-P-0822]

Determination That AVALIDE (Hydrochlorothiazide and Irbesartan), Oral Tablets, 25 Milligrams/300 Milligrams and 12.5 Milligrams/75 Milligrams, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined that AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 milligrams (mg)/300 mg and 12.5 mg/75 mg, were not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for hydrochlorothiazide and irbesartan, oral tablets, 25 mg/300 mg and 12.5 mg/75 mg, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the "listed drug," which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA). The only clinical data required in an ANDA are data to show that the drug that is the subject of the ANDA is bioequivalent to the listed drug.

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the "Approved Drug Products With Therapeutic Equivalence Evaluations," which is known generally as the "Orange Book." Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg and 12.5 mg/75 mg, are the subject of NDA 20-758, held by Sanofi-Aventis, and initially approved

on September 30, 1997. AVALIDE is indicated for treatment of hypertension in patients whose blood pressure is not adequately controlled on monotherapy. AVALIDE is also indicated for initial therapy for hypertension in patients who are likely to need multiple drugs to achieve their blood pressure goals.

AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg and 12.5 mg/75 mg are currently listed in the "Discontinued Drug Product List" section of the Orange Book.

EAS Consulting Group, LLC on behalf of Aurobindo Pharmaceuticals, Ltd. submitted a citizen petition dated October 11, 2011 (Docket No. FDA-2011-P-0743), under § 10.30 (21 CFR 10.30), requesting that the Agency determine whether AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg, were withdrawn from sale for reasons of safety or effectiveness. In addition, Lupin Pharmaceuticals, Inc. submitted a citizen petition dated November 10, 2011 (Docket No. FDA-2011-P-0822), under § 10.30, also requesting that the Agency determine whether AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg, were withdrawn from sale for reasons of safety or effectiveness. Although the citizen petitions did not address the 12.5 mg/75 mg strength, that strength has also been discontinued. On our own initiative, we have also determined whether that strength was withdrawn for safety or effectiveness reasons.

After considering the citizen petitions and reviewing Agency records, and based on the information we have at this time, FDA has determined under § 314.161 that AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg and 12.5 mg/75 mg were not withdrawn for reasons of safety or effectiveness. The petitioners have identified no data or other information suggesting that AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25

mg/300 mg and 12.5 mg/75 mg were withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg and 12.5 mg/75 mg from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have reviewed the available evidence and determined that AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg and 12.5 mg/75 mg were not withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg and 12.5 mg/75 mg, in the "Discontinued Drug Product List" section of the Orange Book. The "Discontinued Drug Product List" delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to AVALIDE (hydrochlorothiazide and irbesartan), oral tablets, 25 mg/300 mg and 12.5 mg/75 mg, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: January 5, 2012.

Leslie Kux,

Acting Assistant Commissioner for Policy.

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